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Relation of fibre intake to HbA_{1c} and the prevalence of severe ketoacidosis and severe hypoglycaemia

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Summary The effect of dietary fibre intake on glycaemic control is still controversial. This study analysed the intake of natural dietary fibre in patients with Type I diabetes mellitus enrolled in the EURODIAB IDDM Complications Study to determine any associations with HbA_{1c} levels and with the prevalence of severe ketoacidosis or severe hypoglycaemia. Dietary intake was assessed by a 3-day dietary record. The relation between intake of fibre (total, soluble and insoluble) and HbA_{1c} was examined in 2065 people with Type I diabetes. Associations with severe ketoacidosis (requiring admission to hospital) and severe hypoglycaemia (requiring the help of another person) were analysed in 2687 people with Type I diabetes. Total fibre intake (g/day) was inversely related to HbA_{1c} ($p = 0.02$), independently of carbohydrate intake, total energy intake and other factors regarding lifestyle and diabetes management. Severe ketoacidosis risk fell significantly with higher fibre intake ($p = 0.002$), with an adjusted odds ratio of 0.48 (95 % confidence interval 0.27 to 0.84) in the highest quartile (≥ 23.0 g fibre/day) compared with the lowest quartile (≤ 13.7 g fibre/day). The occurence of severe hypoglycaemia was not related to fibre intake. Beneficial effects of fibre on HbA_{1c} and the risk of severe ketoacidosis were particularly pronounced in patients from southern European centres. This study shows that higher fibre intake is independently related to a reduction in HbA_{1c} levels in European people with Type I diabetes. Furthermore, increased fibre intake may reduce the risk of severe ketoacidosis. These beneficial effects were already observed for fibre intake within the range commonly consumed by people with Type I diabetes. [Diabetologia (1998) 41: 882–890]

Keywords Fibre intake, soluble fibre, insoluble fibre, HbA_{1c}, severe ketoacidosis, severe hypoglycaemia, Type I diabetes mellitus, Europe.

The Diabetes and Nutrition Study Group of the European Association for the Study of Diabetes encourages people with diabetes mellitus to consume their carbohydrates preferably by means of foods rich in soluble fibre [1]. In this way they can benefit from the positive effects of soluble fibre on blood lipid values as well as on glycaemic control. Health agencies in Europe and North America generally recommend that people with diabetes eat 20–40 g of fibre per day [1–5]. However, in the EURODIAB IDDM Complications Study, a sample of 2868 European patients with Type I diabetes was found to ingest on average 18 g of fibre per day, and the mean daily consumption in the 30 participating centres ranged from 14.7–23.2 g [6].

Over past years there has been controversy over any beneficial effects of dietary fibre on glycaemia. Although short-term studies in subjects with diabetes

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This paper is dedicated to the 95th birthday of Prof. Dr. Karl Oberdisse, the first editor of *Diabetologia*. We as a group would like to follow the tradition and research coined by him and his co-workers.

have shown that a postprandial reduction in blood glucose concentrations can be expected from high-fibre diets – predominantly since viscous gel-forming fibre slows the absorption of ingested carbohydrates – the American Diabetes Assocation concludes that the long-term reduction of blood glucose concentrations associated with diets rich in dietary fibre is probably insignificant [2, 7, 8].

This controversy arose from clinical studies in the 1980s conducted to investigate whether diets containing high amounts of fibre from ordinary food can reduce glycaemia in people with both Type I and Type II diabetes mellitus. Several studies (duration 2 weeks to 15 months) found that an increase in natural fibre intake from 14–30 g to 31–97 g per day resulted in significantly lower blood glucose concentrations or HbA_{1c} levels [9–19]. Conversely, other studies (duration 4 weeks to 19 months) reported that increasing the daily fibre consumption from 20–28 g to 32–50 g of natural fibre had no effect on blood glucose or HbA_{1c} values [20–22]. However, it is difficult to compare these studies because the types and sources of the fibre consumed varied. Moreover, studies were conducted in small samples of 6 to 40 patients.

As near-normal glycaemia can effectively reduce the risk of microvascular and neuropathic complications in people with Type I diabetes [23–25], potential beneficial effects of natural dietary fibre on blood glucose concentrations should be further explored in larger studies. Furthermore, although the goals for good glycaemic control include the avoidance of acute complications such as severe ketoacidosis or severe hypoglycaemia, the effect of dietary fibre intake on these severe acute complications is largely unknown.

This study aims to examine the intake of natural dietary fibre reported by outpatients enrolled in the EURODIAB IDDM Complications Study for possible relations with HbA_{1c} values and prevalence of severe ketoacidosis or severe hypoglycaemia.

Subjects and methods

Subjects. The EURODIAB IDDM Complications Study – a cross-sectional, clinic-based study including 3250 people with Type I diabetes from 31 European centres – has determined the prevalence of diabetic complications and examined established and putative risk factors related to these complications [26]. In each centre a random sample of individuals aged 15–60 years with Type I diabetes was selected from defined strata in relation to gender, age, and diabetes duration. Details of the patient selection procedure have been published [26].

Ethics. The study conformed to the Declaration of Helsinki, and the study protocol was approved by local ethical committees in each centre. Informed consent was given by all patients.

Methods. The standardised nutrition assessment used here has been shown to provide highly reliable nutritional data [27]. Furthermore, plausible energy intakes recorded by 90 % of the patients support the validity of the standardised 3-day dietary record (two workdays, one Sunday) [27]. The specific assessment procedure is described in detail elsewhere [6, 28]. In brief, all food records completed by the patients with Type I diabetes according to standardised instructions were coded by the local dietitian using a centrally prepared EURODIAB food list. At the Nutrition Co-ordinating Centre, diaries were re-checked for completeness and plausibility and then computed. For the present nutritional analysis, data for soluble and insoluble fibre available from European food lists were appended to the previously used EURODIAB nutrient database [29, 30]. The data for the insoluble fibre fraction comprise values from cellulose, insoluble non-cellulotic polysaccharides and lignin, while the soluble fibre data consist of values from soluble non-cellulotic polysaccharides [29, 30]. Dietary records were analysed for intake of fibre (total fibre, soluble fibre, insoluble fibre), carbohydrate, fat (total fat, saturated fat, cholesterol), protein, alcohol and energy.

Blood samples for the measurement of HbA_{1c} were collected, stored and transported according to a standardised procedure described in the EURODIAB manual of operations. HbA_{1c} values were determined in a central laboratory in London (the Royal London Hospital) by an enzyme immunoassay, with a notably low normal range of 2.9 to 4.8 % [31].

Definitions of severe ketoacidosis and severe hypoglycaemia were based on information obtained from a questionnaire completed by all subjects [26, 32]. All patients were asked: "Over the past year, how many episodes of ketoacidosis have occurred requiring hospital admission?" and "Over the past year, how many hypoglycaemic attacks have you had, serious enough to require the help of another person?" Throughout the paper, the occurrence of at least one event per year is referred to as the prevalence of severe ketoacidosis or severe hypoglycaemia. In Bucharest, 50.4 % of the patients reported admission to hospital for ketosis in the past 12 months, while the prevalences observed in the other European centres ranged from 0.8 to 16.7 % [26], depending on whether the centre predominantly cared for patients with specific problems or whether patients were routinely treated in the centre. However, the high prevalence in Bucharest suggests that patients from this centre were more readily admitted to hospital – possibly when they presented with ketone bodies in the urine. We decided to exclude patients from Bucharest from the present analyses to avoid potential bias.

The questionnaire completed by all individuals with Type I diabetes also provided information on physical activity, smoking habits, the frequency of insulin injections, the use of human insulin and the number of daily insulin units injected per kg body weight.

Statistical analysis. Mean daily intakes of energy and nutrients were calculated from the 3-day records. Because normal probability plots showed that distributions for the concentrations of HbA_{1c} and the intake of total energy and fibre (total fibre, soluble and insoluble fibre) were skewed, these variables were log-transformed before statistical analysis.

To assess the relation between fibre intake and its potential confounding factors, the distribution of fibre intake was grouped in quartiles. A test for trend in the confounding factor across quartiles was then performed using the Cochran-Mantel-Haenszel test or analysis of variance for categorical and continuous variables, respectively.

The associations between fibre intake and HbA_{1c} were analysed by least square regression. Mean HbA_{1c} values calculated for each quartile of fibre intake were adjusted for total energy intake [33] and carbohydrate intake (% of energy) to

account for confounding introduced by potential associations of these covariates with HbA_{1c}. In a further step, other parameters possibly related to HbA_{1c} – self-reported alcohol consumption (none, < 20 g and ≥ 20 g per day), frequent meals (≥ 6 times per day), body mass index (BMI) > 25 kg/m^2, diabetes duration, frequent insulin injections (≥ 3 times per day), smoking status (never, past, current) and vigourous exercise at least once a week – were entered in the model. The frequency of meals was treated as a dichotomous variable since about 60 % of the patients ate six meals per day. Furthermore, BMI was entered as a categorical variable since fibre intake was related to BMI > 25 kg/m^2 rather than to the continuous variable. The adjusted means were the values predicted by the model when the other variables were held at their mean value.

Logistic regression was used to determine the odds ratios for severe ketoacidosis and severe hypoglycaemia in quartiles of fibre intake. The key confounding factors considered were total energy intake, carbohydrate intake, self-reported alcohol consumption, frequent meals, presence of BMI > 25 kg/m^2, frequent insulin injections, smoking status and physical activity. In logistic regression models with severe hypoglycaemia, saturated fat intake (% of energy) and use of human insulin were also accounted for.

For region-specific analyses the participating centres were grouped as follows: *southern European centres* – Athens, Bari, Cagliari, Lisbon, Milan, Perugia, Pisa, Rome, Turin, Thessaloniki and Verona; *eastern European centres* – Budapest, Krakow and Zagreb; *north-western European centres* – Cork, Düsseldorf, Gent, Helsinki, Leiden, London, Luxembourg, Manchester, Munich, Paris, Sheffield, Valenciennes, Vienna and Wolverhampton.

In this study, patients from Bucharest (n = 139) and patients taking oral hypoglycaemic agents (n = 18) were excluded. Thus, models analysing fibre intake in relation to severe ketoacidosis or severe hypoglycaemia are based on 2687 subjects (1366 men, 1321 women). Since some centrally measured HbA_{1c}-concentrations were missing from all centres, only 2065 individuals with Type I diabetes (1051 men, 1014 women) could be included in the study of the relation between fibre intake and HbA_{1c} concentrations.

All statistical analyses were carried out using the SAS program [34].

Table 1. Characteristics of 2065 patients with Type I diabetes

Age (years)[a]	32.7 (10.2)
Diabetes duration (years)[a]	14.8 (9.5)
HbA_{1c} (%)[b]	6.4 (1.9–15.5)
Total fibre intake (g/day)[b]	17.7 (2.6–63.4)
Soluble fibre intake (g/day)[b]	5.6 (0.8–20.2)
Insoluble fibre intake (g/day)[b]	12.0 (1.8–43.8)
Total energy intake (kcal)[b]	2289 (670–5510)
Carbohydrate intake (% of energy)[a]	42.3 (7.3)
Gender (% males)	50.9
Self-reported alcohol intake:	
No intake (%)	49.5
< 20 g/day (%)	37.9
≥ 20 g/day (%)	12.6
Frequent meals (≥ 6 times/day) (%)	59.1
BMI > 25 kg/m^2 (%)	25.9
Frequent insulin injections (≥ 3 times/day) (%)	50.8
Use of human insulin (%)	87.4
Current smokers (%)	33.2
Ex-smokers (%)	17.6
Vigorous exercise at least once a week (%)	14.0

[a] Mean (SD)
[b] Median (range)

Results

Fibre intake and HbA_{1c}. The 2065 people with Type I diabetes ate a mean of 17.7 g total fibre per day (range: 2.6–63.4 g/day) (Table 1). Overall, 37 % of the subjects had a fibre intake of at least 20 g/day. The median HbA_{1c} was 6.4 % (1.9–15.5 %), a level which would correspond to approximately 8.1 % determined by HPLC. Of the total cohort, 82 % exceeded the upper level of normal of 4.8 %.

The association between fibre intake and levels of HbA_{1c} is presented in Table 2. In bivariate analysis, HbA_{1c} levels were not related to fibre intakes. After adjustment for intake of carbohydrate and total energy, a significant independent trend of HbA_{1c} to fall with higher fibre intakes was observed. The trend was maintained when further confounding factors were accounted for. Separate analysis of soluble and insoluble fibre yielded a significant inverse association with HbA_{1c} levels for both fibre fractions (Table 2).

In multivariate stepwise regression, only the soluble fibre fraction was found to significantly predict HbA_{1c} levels (p = 0.02).

Figure 1 shows that in the southern European centres HbA_{1c} values fell significantly with higher quartiles of total or soluble fibre intake. For the eastern European centres, only the inverse relation between HbA_{1c} and soluble fibre intake reached significance. In the western European centres, HbA_{1c} was lower in all quartiles, irrespective of total or soluble fibre intake.

When a further term for units of insulin per kg body weight was included in the models the results were comparable.

Fibre intake, severe ketoacidosis and severe hypoglycaemia. Of the 2687 patients with Type I diabetes included in the analysis, 166 (6.2 %) had experienced at least one episode of severe ketoacidosis that required admission to hospital over the past year. Severe episodes of hypoglycaemia that required the help of another person were reported by 854 (31.8 %) study subjects.

Potential confounding factors for severe ketoacidosis or severe hypoglycaemia in relation to quartiles of total fibre intake are given in Table 3. Patients with higher intakes of fibre consumed more total energy, more carbohydrate (% of energy) and less saturated fat (% of energy). In the upper quartiles of fibre in-

Table 2. Mean HbA_{1c}[a] in categories of fibre intake for 2065 patients with Type I diabetes

Quartiles Median intake (range)	Bivariate analysis	Adjustment for intakes of carbohydrate and energy	Full model[b]
Total fibre intake (g/day) [a]			
11.4 (2.6–13.6)	6.38 (6.23, 6.55)	6.54 (6.36, 6.73)	6.50 (6.32, 6.68)
15.6 (13.6–17.7)	6.38 (6.23, 6.55)	6.43 (6.27, 6.59)	6.42 (6.26, 6.58)
20.0 (17.7–22.8)	6.32 (6.16, 6.48)	6.27 (6.12, 6.44)	6.29 (6.13, 6.45)
27.3 (22.8–63.4)	6.33 (6.17, 6.49)	6.18 (6.01, 6.35)	6.21 (6.04, 6.39)
Trend	$p = 0.6$	$p = 0.003$	$p = 0.02$
Soluble fibre intake (g/day) [a]			
3.5 (0.8–4.3)	6.33 (6.17, 6.49)	6.48 (6.30, 6.66)	6.43 (6.25, 6.61)
4.9 (4.3–5.6)	6.41 (6.25, 6.58)	6.45 (6.29, 6.62)	6.45 (6.30, 6.62)
6.3 (5.6–7.2)	6.35 (6.20, 6.52)	6.32 (6.16, 6.48)	6.33 (6.18, 6.49)
8.9 (7.2–20.2)	6.32 (6.16, 6.48)	6.17 (6.00, 6.35)	6.21 (6.04, 6.38)
Trend	$p = 0.6$	$p = 0.003$	$p = 0.02$
Insoluble fibre intake (g/day)[a]			
7.6 (1.8–9.1)	6.43 (6.27, 6.59)	6.59 (6.41, 6.77)	6.54 (6.36, 6.72)
10.6 (9.2–12.0)	6.36 (6.21, 6.53)	6.41 (6.25, 6.58)	6.40 (6.24, 6.56)
13.5 (12.0–15.5)	6.30 (6.15, 6.46)	6.26 (6.10, 6.42)	6.29 (6.13, 6.44)
18.7 (15.5–43.8)	6.32 (6.17, 6.48)	6.17 (6.00, 6.34)	6.20 (6.03, 6.37)
Trend	$p = 0.6$	$p = 0.005$	$p = 0.03$

[a] Log-transformed
[b] Adjusted for potential confounding factors discussed in *Methods* and listed in Table 3

take, the percentages of people who ate six or more meals per day were higher and fewer individuals had a BMI > 25 kg/m^2. The quartiles of higher fibre intake included more physically active people and fewer smokers.

The prevalence of severe ketoacidosis fell significantly with higher intakes of total fibre, soluble fibre and insoluble fibre (Table 4). Adjustment for potential confounding factors further enhanced the observed relation. The risk of a severe episode of hypoglycaemia was not significantly reduced in the higher

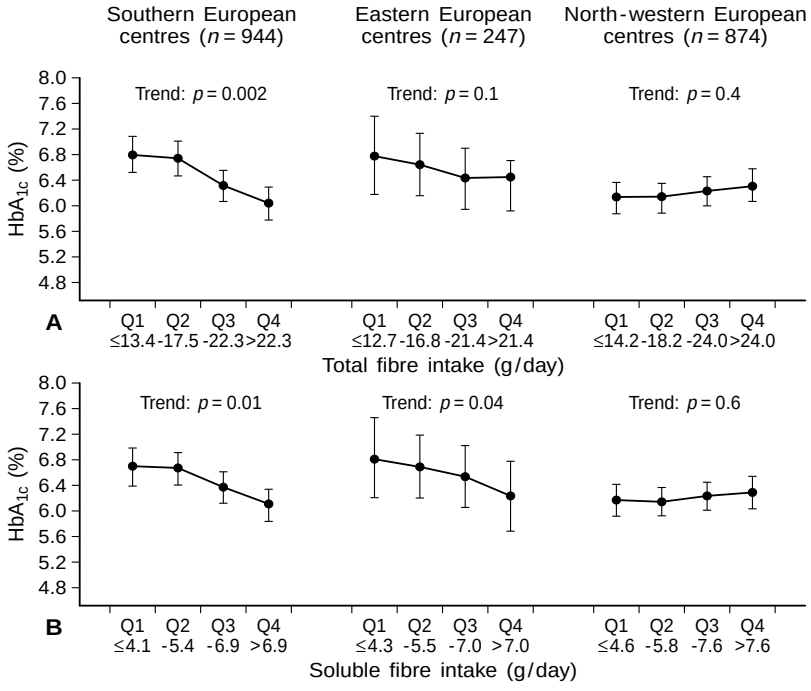

Fig. 1. (**A**) Geometric mean HbA_{1c} in relation to quartiles of total fibre intake for people with Type I diabetes from different European regions. (**B**) Geometric mean HbA_{1c} in relation to quartiles of soluble fibre intake for people with Type I diabetes from different European regions. Mean HbA_{1c} levels (95 % CI) are adjusted for the confounding factors discussed in *Methods* and in Table 3

Table 3. Potential confounding factors for severe ketoacidosis and severe hypoglycaemia in relation to quartiles of total fibre intake in 2687 European people with Type I diabetes

	Quartiles of fibre intake (g/day) (median (range))				
	1st 11.4 (2.6–13.7)	2nd 15.6 (13.7–17.8)	3rd 20.1 (17.8–23.0)	4th 27.4 (23.0–63.4)	*p* value for trend[a]
Energy (kcal) (median (range))	1939 (513–4655)	2170 (937–5415)	2370 (825–5175)	2774 (949–6423)	0.0001
Carbohydrate (% of energy)	38.8 (7.1)	41.6 (6.7)	43.6 (6.7)	46.2 (6.8)	0.0001
Saturated fatty acids (% of energy)	15.0 (3.4)	14.3 (3.2)	13.6 (3.5)	12.7 (3.3)	0.0001
Self-reported alcohol consumption					
No intake (%)	51.0	49.3	48.8	52.2	0.7
< 20 g/day (%)	36.0	37.6	41.1	36.2	0.6
≥ 20 g/day (%)	12.9	13.1	10.1	11.6	0.2
Frequent meals (≥ 6 times/day) (%)	47.6	58.5	66.1	69.9	0.001
BMI > 25 kg/m^2 (%)	30.1	27.8	26.6	24.7	0.03
Frequent insulin injections (≥ 3 times/day) (%)	51.8	49.1	50.7	52.9	0.6
Use of human insulin (%)	85.0	86.3	86.9	88.1	0.1
Current smokers (%)	41.8	35.1	29.9	25.3	0.001
Ex-smokers (%)	14.9	16.7	18.2	20.6	0.01
Vigorous exercise at least once a week (%)	9.7	12.2	15.2	18.2	0.001

[a] Variance analysis and Mantel-Haenzel X^2-test

Table 4. Crude and adjusted odds ratios (OR) for severe ketoacidosis and severe hypoglycaemia by categories of fibre intake in 2687 individuals with Type 1 diabetes

Quartiles (median intake (range))	Severe ketoacidosis			Severe hypoglycaemia		
	Crude rates *n* (%)	Crude OR	Adjusted OR[a]	Crude rates *n* (%)	Crude OR	Adjusted OR[a]
Total fibre intake (g/day)						
11.4 (2.6–13.7)	52 (7.7)	1	1	223 (33.2)	1	1
15.6 (13.7–17.8)	42 (6.3)	0.80 (0.52, 1.21)	0.76 (0.49, 1.18)	202 (30.1)	0.87 (0.69, 1.09)	0.82 (0.64, 1.04)
20.1 (17.8–23.0)	39 (5.8)	0.74 (0.48, 1.13)	0.65 (0.40, 1.04)	214 (31.9)	0.94 (0.75, 1.18)	0.84 (0.65, 1.09)
27.4 (23.0–63.4)	33 (4.9)	0.62 (0.39, 0.97)	0.48 (0.27, 0.84)	215 (32.0)	0.95 (0.76, 1.19)	0.80 (0.60, 1.07)
Trend		$p = 0.02$	$p = 0.002$		$p = 0.8$	$p = 0.3$
Soluble fibre intake (g/day)						
3.5 (0.8–4.3)	52 (7.7)	1	1	220 (32.7)	1	1
4.9 (4.3–5.6)	45 (6.7)	0.86 (0.57, 1.30)	0.78 (0.50, 1.20)	206 (30.7)	0.91 (0.72, 1.14)	0.85 (0.67, 1.08)
6.4 (5.6–7.2)	35 (5.2)	0.66 (0.42, 1.02)	0.58 (0.35, 0.94)	213 (31.7)	0.95 (0.76, 1.20)	0.85 (0.66, 1.10)
8.8 (7.2–20.2)	34 (5.1)	0.64 (0.41, 0.99)	0.45 (0.26, 0.80)	215 (32.0)	0.97 (0.77, 1.22)	0.80 (0.60, 1.08)
Trend		$p = 0.04$	$p = 0.003$		$p = 0.9$	$p = 0.2$
Insoluble fibre intake (g/day)						
7.7 (1.8–9.2)	53 (7.9)	1	1	221 (32.9)	1	1
10.6 (9.2–12.1)	41 (6.1)	0.76 (0.50, 1.16)	0.75 (0.49, 1.17)	201 (29.9)	0.87 (0.69, 1.10)	0.84 (0.66, 1.06)
13.6 (12.1–15.6)	40 (6.0)	0.74 (0.48, 1.13)	0.66 (0.41, 1.07)	213 (31.7)	0.95 (0.75, 1.19)	0.87 (0.68, 1.12)
18.8 (15.6–43.8)	32 (4.8)	0.59 (0.37, 0.92)	0.47 (0.27, 0.82)	219 (32.6)	0.99 (0.79, 1.24)	0.87 (0.65, 1.16)
Trend		$p = 0.02$	$p = 0.002$		$p = 0.7$	$p = 0.4$

[a] Adjusted confounding factors discussed: *Methods* and listed in Table 3

quartiles of fibre intake, even when potential confounding factors were adjusted for.

In stepwise logistic regression, only the insoluble fibre fraction was found to predict significantly the risk of severe ketoacidosis ($p = 0.002$).

Figure 2 illustrates the risk of severe ketoacidosis in relation to region-specific quartiles of total fibre and insoluble fibre. In the southern European centres, adjusted odds ratios fell significantly with higher intakes of total and insoluble fibre. A similar trend could be observed for the eastern European centres, but it did not reach statistical significance. Conversely, in the north-western European centres the prevalence of severe ketoacidosis was low in all quartiles, irrespective of total or insoluble fibre intake.

Further adjustment for units of insulin per kg body weight yielded similar results. When analyses were repeated for the 2065 individuals with Type I diabetes for whom centrally measured HbA_{1c} values were available, similar trends were observed. Further ad-

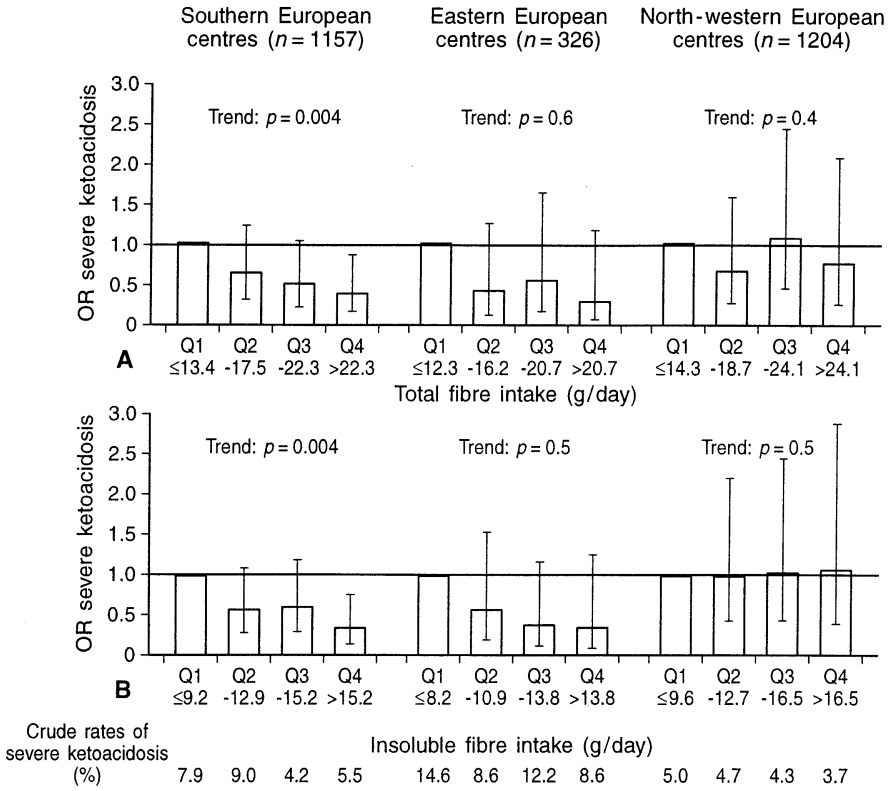

Fig. 2. (**A**) Odds ratios for severe ketoacidosis in relation to quartiles of total fibre intake for people with Type I diabetes from different European regions. (**B**) Odds ratios for severe ketoacidosis in relation to quartiles of insoluble fibre intake for people with Type I diabetes from different European regions. Odds ratios (95% CI) for severe ketoacidosis are adjusted for the confounding factors discussed in *Methods* and in Table 3

justment for HbA_{1c} did not materially change the results.

Discussion

In this study, fibre intake of a large cohort of European subjects with Type I diabetes was analysed to determine any relation to glycaemic control. Our results show that intake of fibre (supplied by a broad range of locally available foods) is significantly related to levels of HbA_{1c} in insulin-treated-European patients, independently of carbohydrate and total energy intake. The mechanism whereby the increased fibre intake beneficially affects HbA_{1c} presumably relates to reduced postprandial blood glucose peaks. Thus, an increased fibre intake may contribute to an overall improvement of glycaemic control, but can certainly not replace insulin.

Correlations of natural fibre intake with levels of HbA_{1c} have also been reported from other observational studies in patients with Type I diabetes [35–37]. In multivariate analyses, however, fibre intake was not an important predictor for HbA_{1c} [35, 37]. These studies did not adjust simultaneously for carbohydrate intake. Yet, several clinical studies in diabetic people suggest that beneficial effects on levels of HbA_{1c} observed with diets rich in both carbohydrate (53–65% of total energy) and dietary fibre (45–54 g/day) result from the natural dietary fibre rather than the amount of carbohydrate [9, 14, 15, 38]. Increasing carbohydrate intake without simultaneously increasing the intake of dietary fibre may even worsen glycaemic control [15]. Thus, adjustment for carbohydrate is needed in order to disentangle the potentially opposing effects of carbohydrate and fibre intakes on levels of HbA_{1c}.

Benefits of natural dietary fibre on glycaemic control have been ascribed primarily to the viscous gel-forming soluble fibre fraction [7, 38, 39]. In this large group of people with Type I diabetes we saw an association between fibre intake and HbA_{1c} for both the soluble and the insoluble fibre fraction. However, when both fibre types were included in the statistical model, only soluble fibre was related to levels of HbA_{1c}. It therefore seems that the association of insoluble fibre and HbA_{1c} observed in this study largely reflects the high correlation between soluble and insoluble fibre intakes.

Effective reduction in glycaemia by high-fibre diets have been observed, particularly in clinical studies using a traditional Mediterreanean diet with about 50 g of natural dietary fibre [14, 15, 38]. After a period of 2 weeks both the fasting and the 2 h post-

prandial blood glucose concentrations of patients with Type I diabetes were reduced by 2–3 mmol/l. In this study, the examination of regional patterns showed a significant relation between the intake of total or soluble fibre and levels of HbA_{1c} for the centres in southern and eastern Europe. In centres in north-western-Europe no association between fibre intake and HbA_{1c} was found, and this overall lack of a relation was seen consistently in all these centres. This discrepancy may be partly explained by different sources or composition of the foods supplying the fibre in the respective region, or by different glycaemic indices of the diets [9, 10, 12, 17, 38–40]. These aspects were not analysed here. However, mean levels of HbA_{1c} in the north-western European centres were lower than in eastern or southern European centres, possibly since structured self-care programmes were established in many centres in north-western Europe at the beginning of the 1980s and may have resulted in a lower HbA_{1c}. Thus, higher fibre intakes may have less potential to improve glycaemic control further in patients who have already achieved good glycaemic control.

To our knowledge, this is the first study to investigate potential associations of fibre intake and severe ketoacidosis or severe hypoglycaemia. Ketoacidosis requiring admission to the hospital is a severe, potentially lethal diabetic complication [41]. Despite decreasing prevalences of ketoacedotic coma in Europe over past decades [41], many study subjects with Type I diabetes still reported one or more episodes of severe ketoacidosis that needed hospital treatment. Thus, a further reduction in the prevalence of severe ketoacidosis is crucial. Severe hypoglycaemia is also an acute complication that represents a continuous threat to most people with Type I diabetes [32, 41–43]. In this study, the definitions of severe ketoacidosis and severe hypoglycaemia rely on the patient's self-report in a standardised questionnaire, and thus carries some risk of misclassification. However, we believe that people with Type I diabetes will be able to remember accurately an acute episode of hypoglycaemia so severe that they could not overcome it alone or a ketosis so severe that it needed admission to the hospital.

Our data suggest that moderate increases in fibre intake – preferably to levels above 20 g/day – may reduce the risk of severe ketoacidosis, but not that of severe hypoglycaemia. Thus, a lower mean glycaemia value associated with increased fibre intake may also translate into an overall reduction in severely high blood glucose concentrations, thus reducing the risk of ketoacidosis. Potential confounding factors characterising a more health-conscious lifestyle – in the present study, associated with a higher fibre intake – did not explain the relation between fibre intake and the risk of severe ketoacidosis. On the contrary, the adjustments even enhanced the observed association. However, we cannot rule out the possibility that the observed relation partly reflects an assocation between the occurence of severe ketoacidosis and regular self-monitoring or self-adjustment of insulin, or both, as these aspects were not assessed in detail in this cross-sectional study.

Sources and types of dietary fibre may vary according to national, regional and cultural influences. The large variety of dietary patterns allows us to determine diet-disease relation in large multi-centre studies. Thus, adjustment for country or centre, or both, which accounts for these regional variations, could result in an underestimation of the true association between dietary fibre and glycaemic control [44]. Instead, we carried out region-specific analyses to examine regional variations in the observed associations. In our initial nutrition analysis, we had observed regional differences in the nutrient intake pattern of the European patients with Type I diabetes [6]. Based on these geographical variations, centres from southern Europe, eastern Europe or north-western Europe were grouped for the region-specific analysis in this study. Within each region, centre-specific findings were broadly in the same direction. We are, however, aware that no general conclusions for European regions can be drawn from our analyses as the distribution of the centres is not representative of the respective European regions.

The tendency of the risk of severe ketoacidosis to fall in higher quartiles of total and insoluble fibre intake was most pronounced for the southern European centres, but, also evident (though not significant) for the eastern European centres. However, no association could be observed in the north-western European centres, where severe ketoacidosis was reported by only 4% of the subjects with Type I diabetes. Thus, higher fibre intake does not seem to provide much additional protection for groups of patients in whom severe ketoacidosis is a less common diabetic complication.

In conclusion, this study shows significant, independent inverse associations between fibre intake and levels of HbA_{1c} and with the risk of severe ketoacidosis in European people with Type I diabetes. These beneficial effects were already observable for the amounts of fibre commonly consumed throughout Europe by study subjects with Type I diabetes. More attention should be directed towards increasing fibre intake moderately, preferably to more than 20 g of natural dietary fibre. Confirmation of our results by further large studies would be desirable.

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